National Institute of Allergy and Infectious Diseases

NIAID Council News

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Budget News Is Good for Now

NIAID is looking at a very bright budget picture for the short term.

As we reported in our last newsletter issue, Congress appropriated 7.6 percent more money to the Institute in FY 1997 than it did last year.

This hefty influx of funds enabled NIAID to craft its FY 1997 funding policy.

- Payline at the 24.0 percentile for non-AIDS applications, 26.0 for AIDS.
- Payline at 32.0 for FIRST (R29) awards.
- 3.0 percent inflationary increases to existing grants.
- Bridge awards to continue.

In a move benefiting applicants, NIAID raised the paylines (initial funding cutoff points) in March *retroactive to October, the beginning of the fiscal year.*

Last year's paylines were 18.0 for non-AIDS, and 22.0 for AIDS.

Another rising indicator, our success rate, is expected to increase from last year's 31.7 percent to about 32.6 percent in FY 1997.

Inside

GRANTS & review

Bridge Awards Get Even Better

NIAID will continue its popular bridge program next year with two new features.

After hearing positive comments from Council in January, NIAID will go forward with these changes:

- Awards to be made throughout the year.
- Funding to be based on Council's advice.

The changes are being phased in and will be fully implemented by September.

Last year because of the program's late start, NIAID made bridge awards at the end of the fiscal year and chose recipients in strict percentile order. Investigators do not apply for bridge awards but are selected from R01 and R29 grants at the payline margin.

Bridge awards provide one year of funding so investigators can continue research while reapplying for a grant renewal.

They also enable new investigators to gather preliminary data to improve their applications.

The amount of money dedicated to the program will depend on NIAID's final budget level for this fiscal year.

Testing Potential Review Rating Criteria

Against a backdrop of recommendations from an NIH committee and public feedback, NIAID is continuing to test new measures for rating grant applications.

Begun last fall, these test pilots are trying out potential new rating criteria, their applicability to different grant types, and the benefit of assigning individual ratings to each criterion.

NIH still undecided

Meanwhile, discussions at NIH to define standard review criteria are still going on.

At the February 13 meeting of the Peer Review Oversight Group (PROG), NIH did not reach consensus on what the new criteria should be.

The group decided to recommend to Dr. Varmus the use of three or four criteria: impact, approach, and investigator/environment with the possible addition of creativity as a fourth criterion.

NIH hopes to finalize the specific criteria and their use by next year.

NIAID pilot of potential rating criteria

During October and November, NIAID's Scientific Review Program tested a set of three review criteria—impact, approach, and feasibility—very similar to those recommended by PROG several months later.

Fifty-three reviewers participated in the pilot, reviewing 46 applications of various types (see box below).

To garner feedback, we distributed a questionnaire, which was returned by 72 percent of the reviewers (see box on the next page for data on the results).

No computed overall score

Of those responding, 75 percent wanted to assign the overall score themselves rather than have it computed.

Reviewers emphatically rejected using a standard

NIAID Rating Criteria Pilot —Application Types

Program projects

Career development awards

Conference grants

Research and demonstration awards

weighting or algorithm to derive a final score from the individual scores.

No single criterion emerged as the most influential on the overall score.

Interestingly, reviewers overwhelmingly favored having their own applications reviewed under the new criteria.

One reviewer commented, "I can't wait to have my application reviewed this way. I want reviewers to think about the impact of my work as well as the approach and feasibility."

General assessment positive

Most reviewers were satisfied with the new criteria.

They felt that placing more emphasis on impact was positive but preferred folding it into creativity rather than making it a separate criterion.

Further, most reviewers thought the quality and focus of the discussions were helped by these criteria and expected summary statements to convey results more effectively.

Though the pilot criteria increased reviewers' preparation time and the length of discussions at the meeting, this was probably due to the volume of new information they had to assimilate.

Once the learning period is over, the time difference will likely diminish.

Reviewers also felt that the criteria benefited the reviews regardless of grant type.

Our trials were led by Drs. Christopher Beisel, Kevin Callahan, Hortencia Hornbeak, Gary Madonna, Olivia Preble, and Diane Tingley.

SBIR Applications Now Undergo Streamlined Review

This year, NIH will begin using streamlined review procedures for Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) applications.

This change will be reflected in the FY 1997 SBIR and STTR solicitations (both are available on the Web at http://www.nih.gov/grants/funding/sbir.htm).

NIH adopted streamlined review (formerly known as triage) for research project (R01) and some other grant types in 1995; NIAID has been using it since 1986.

Under this system, only applications judged by the study section to be highly meritorious—roughly the top 50 percent—are discussed and scored by the scientific review group.

For those in the bottom tiers—unscored applications—applicants receive a copy of the reviewers' critiques but not a full summary statement or priority score (for a discussion of review designations, see the article on page 10).

NIAID Rating Criteria Pilot—Reviewer Responses

Over 50 percent of reviewers thought the discussion was better using the new criteria.*

About 33 percent of reviewers thought it was the same.

75 percent of reviewers did not want to separate creativity from impact.

75 percent of reviewers wanted to assign an overall score rather than have it computed from the individual scores.

*Results were the same for all award types.

NIGMS and DRG Pilot NIAID's Electronic Review System

Following NIAID's experiment, the National Institute of General Medical Sciences (NIGMS) did its own test of electronic peer review.

Peer reviewers and staff alike were impressed.

Under the guidance of scientific review administrators (SRA) Drs. Richard Martinez and Michael Sesma, NIGMS used the encrypted Worldwide Web site developed by NIAID to do the groundwork for reviewing training and conference grants.

Most of the premeeting work took place on the Web: the SRAs made assignments and interacted with reviewers. Reviewers entered their critiques, made comments, and raised questions.

Gaining a more thorough review

Reviewers felt that the electronic system gave them the opportunity to look more thoroughly at all aspects of an application.

As Dr. Martinez said, "The electronic forum looks like a tree with many branches. When there are many comments on a set of branches, it immediately highlights an area of concern among reviewers."

He felt that electronic reviews would probably facilitate the evaluation of applications for institutional training programs, such as Minority Access to Research Careers, and also benefit other application types requiring in-depth discussion of technical details, e.g., research project grants (R01).

Changing group dynamics

Certainly, the new venue alters group dynamics. Whereas face-to-face meetings can be dominated by strong personalities, the playing field is leveled somewhat by the electronic format.

Both SRAs felt that the electronic mode may encourage more reticent reviewers to "speak up" and participate more actively, bringing more diverse perspectives into the discussion.

Despite the changes, however, the live meeting is still at the core of the review.

"Remember that the electronic system doesn't replace the face-to-face review, but it does change what happens at the review meeting," Dr. Sesma noted.

For NIGMS, the meeting went very fast, and discussions were extremely well focused.

One drawback being addressed is that reviewers may have spent more time preparing for it.

Easy to use

All reviewers used the system and felt it was easy to master, and both SRAs were "very enthusiastic about the electronic system."

NIAID is making the technology available to any Institute that wants it. Based on the success of these trials, NIGMS is planning to set up its own Web site for reviews.

NIGMS also plans to expand the use of the electronic system to other reviews of training applications and to program projects.

TMP begins electronic review

In NIH's Division of Research Grants, the Tropical Medicine and Parasitology (TMP) study section recently began testing our electronic review system too.

After finishing a trial run that included 16 reviewers, SRA Dr. Jean Hickman noted that the reviewers liked the system, especially being able to access each other's comments before the meeting.

All but two reviewers used the system successfully.

In our next newsletter issue, we will fill you in with more information about the outcome of the TMP trials.

INSTITUTE & staff

New OD Staff Take Permanent Places

Dr. Fauci has decided to make official the staff changes he has been testing out since last fall for his new management team.

John McGowan—Deputy Director, NIAID

Dr. John J. McGowan is NIAID's new deputy director, providing leadership for scientific and extramural policy issues and senior-level interactions with other Institutes and the OD, NIH.

Dr. McGowan came to NIAID in 1986.

One of the first staff members of what is now the Division of AIDS, he put together the Developmental Therapeutics Branch and was later promoted in DAIDS to director of the Basic Research and Development Program.

In 1991, Dr. McGowan became the director of the Division of Extramural Activities.

He was widely recognized in that role for his leadership in designing and implementing many reinvention experiments, working at the NIH and Institute levels.

Before coming here, Dr. McGowan was a grantee studying the molecular biology of rhabdo, corona, and bunya viruses at the Uniformed Services University of the Health Sciences.

He graduated from the University of Mississippi with a Ph.D. in microbiology.

Mr. Steven Berkowitz—Associate Director, NIAID

Now working in another key leadership position is Mr. Steven J. Berkowitz, who has assumed the role of associate director for management and operations.

Having an M.B.A. and C.P.A., Mr. Berkowitz has served as NIAID's chief financial, information systems, and technology transfer officers, assuming more managerial responsibility over the years.

In his new role, Mr. Berkowitz will directly manage several key offices under the Office of the Director and advise Dr. Fauci on program, business, and administrative policy issues.

Mr. Berkowitz has worked at NIH for 16 years in finance, grants accounting, systems analysis, budget, information technology, technology transfer, and policy.

Before coming to NIAID, he worked five years for the General Accounting Office performing internal control reviews and program assessments and responding to congressional requests.

Filling another important position, Mr. Roger E. Pellis is NIAID's new executive officer, directing the Office of Administrative Services.

DAIDS Appoints New Branch Chief

Dr. James G. McNamara is the new chief of the Pediatric Medicine Branch of the Division of AIDS.

Dr. McNamara joined the Division in 1991 as a medical officer in that Branch.

In 1995, he left the Pediatric Medicine Branch to become chief of the Clinical Development Branch of the Vaccine and Prevention Research Program in DAIDS, where he worked until assuming his new position.

Before joining NIAID, Dr. McNamara was on the faculty of the Yale University School of Medicine, where he also completed his pediatric and immunology training.

He received his medical degree from the University of Vermont College of Medicine.

New AIDS Vaccine Committee Takes Its First Steps

David Baltimore, Ph.D., professor of molecular biology and immunology at the Massachusetts Institute of Technology, is chairing a new committee to find opportunities for developing an HIV vaccine.

The Nobel Prize-winning scientist heads the AIDS Vaccine Research Committee, a working group of outside experts looking at promising scientific areas and advising NIH accordingly.

At its first meeting on February 17, the group planned to launch a new small grants program, called "Innovation," to conduct exploratory and developmental research.

The first phase of the pilot program targets three areas of research: the structure and function of the HIV envelope protein, improved animal models for vaccine and pathogenesis studies, and the mechanisms of directing antigen processing *in vivo* to maximize the immune response. For more information about the program, call Dr. Carole Heilman at 301/496-0545.

Administratively linked to the NIAID Council, the Committee will make recommendations to NIAID, the NIH Office of AIDS Research (OAR), and other NIH components on key scientific questions.

Members have diverse scientific expertise, including immunology, structural biology, virology, animal models, and vaccines.

Dr. Baltimore's appointment fulfills a key recommendation of the Levine Panel, which, at the request of the OAR, evaluated NIH's AIDS research programs, issuing a report of its findings in March 1996.

AIDS Vaccine Research Committee

Chair, Dr. David Baltimore

Dr. Barry Bloom
Dr. Robert Couch
Dr. Beatrice Hahn
Dr. Peter Kim
Dr. Norman Letvin
Dr. Daniel Littman
Dr. Douglas Richman
Dr. William Snow
Dr. Irving Weisman

Setting Priorities for Tuberculosis Research

Last November, NIAID invited outside experts to review its tuberculosis research program.

Partly as a result of this group's advice, NIAID will likely modify some of its research directions.

During a full day of presentations, the panel assessed the state of the science and research priorities following NIAID's increased investment in this area—rising from about $10 million in 1992 to over $36 million in 1996 (see graphic next page).

Topics ranged from vaccine and drug development to microbial physiology and immunopathogenesis.

The 10 reviewers and chair, Council member Dr. Robert Couch of the Baylor College of Medicine, developed a set of recommendations, shown on the next page.

Tuberculosis Research Program Review Panel

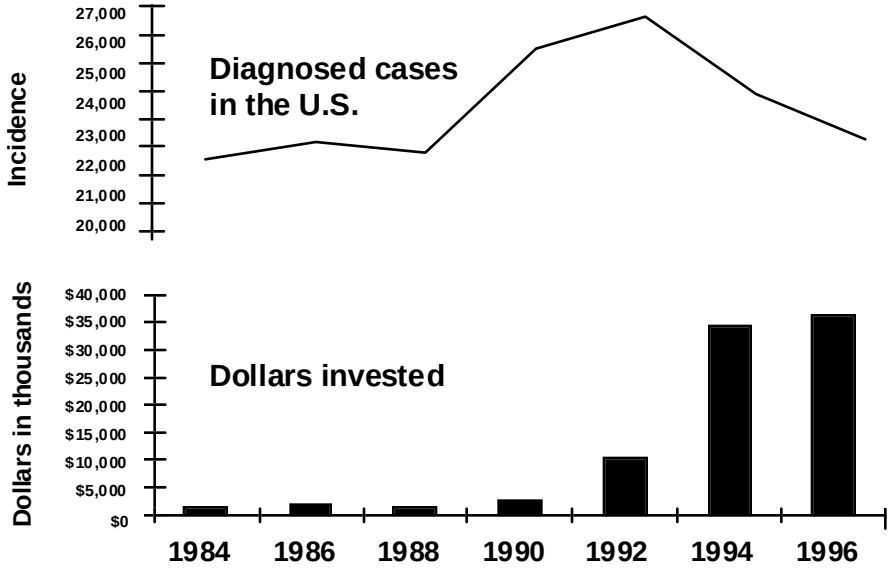
Dr. Robert Couch (chair)
Dr. Michael Apicella
Dr. Joseph Bates
Dr. James Cowell
Dr. Ronald Germain
Dr. Mark Goldberger
Dr. Dennis Kasper
Dr. Carol Nacy
Dr. John Ryan
Dr. Maggie So
Dr. William Stead

Presenters
Dr. Barry Bloom
Dr. Patrick Brennen
Dr. Jerrold Ellner
Dr. Lee Riley
Dr. Peter Small
Dr. Douglas Young

Summary of Panel Recommendations

- Support more basic research of *M. tuberculosis* and its interaction with human cells. In any redirection of funding, emphasize research directly related to human tuberculosis.
- Develop a systematic plan for exploiting genome information.
- Support research of latency.
- Improve diagnostic tools for active and latent disease and tuberculosis in the presence of HIV infection. Coordinate with industry.
- Use knowledge derived from research into the stage of the organism's life cycle to rationally design better therapeutic agents. Periodically review the drug discovery effort to ensure that new basic knowledge is being used.
- Validate the appropriateness of current screening processes and consider alternative approaches.
- Foster vaccine development by supporting basic research in immunology and pathogenesis, studying immune correlates in people, and using a more selective approach to screening vaccine candidates.
- Address the problem of attracting and keeping investigators involved in research that may yield results slowly due to the difficulty in growing and working experimentally with *M. tuberculosis*.
- Continue support for NIAID's Tuberculosis Research Unit.

Meeting the Tuberculosis Challenge



Managed Care Comes to NIH

In sync with sweeping changes in medical care payment arrangements, NIH is now grappling with managed care.

Parts of a recent inspector general report on the NIH Clinical Center have raised concern here, including recommendations to segregate research from nonresearch costs and to charge for nonresearch care.

Dr. John Gallin, director of the NIH Clinical Center, addressed NIAID's Council in September on the changes managed care is making in NIH-conducted and grant-supported research.

Although NIH is committed to treating patients without cost to them, Dr. Gallin said, the Clinical Center has already begun moving toward recruiting patients from managed care organizations with which it has financial arrangements.

NIAID working group

To help NIAID adapt to the increasing role of managed care in research centers, Dr. Fauci set up a working group last fall.

Dr. Lawrence Deyton, acting director of NIAID's Division of Extramural Activities, presented that group's recommendations to Institute management at the recent Winter Policy Retreat.

Recommendations of the NIAID Working Group on Managed Care

Implement clinical trial payment agreements with the Department of Defense.

Discuss possible collaborations between clinical investigators sponsored by NIAID (e.g., AIDS Clinical Trials Groups) and state Medicaid programs to accomplish goals, such as:

- Reduce rates of maternal-fetal HIV transmission by new therapeutic strategies.
- Show the cost effectiveness and efficacy of the Inner-City Asthma protocol and coordinated care approach.
- Improve strategies for childhood vaccines and test new vaccine products.

Initiate discussions with one or two large managed care organizations to stimulate patient referrals for NIAID's research programs.

Support a limited amount of research associated with ongoing projects to explore the impact of managed care on NIAID-supported basic research, clinical trials, and training.

He is also NIAID's representative on an NIH working group chaired by National Heart, Lung, and Blood Institute director Dr. Claude Lenfant, developing procedures for health care beneficiaries covered by the Department of Defense to participate in NIH-sponsored clinical trials.

The NIAID working group's recommendations centered on engaging in several trial collaborations between NIAID-funded scientists and either public or private managed care organizations (see box above).

Caution from Clinical Center review

Early this year, the NIH Clinical Center benefited from the advice of an outside advisory group that, among other topics, explored issues relating to the effects of managed care.

Known as the Options Team, the group felt NIH must work carefully with managed care organizations to protect the integrity of NIH research and patient access and confidentiality, while potentially benefiting from access to patients with conditions under study.

NIH Options Team Recommendations

Segregating nonresearch care is problematic and conflicts with the principles of clinical research.

NIH should explore creative arrangements with large insurers and managed care organizations.

Patient confidentiality must be protected.

NIH should avoid complex fee-for-service arrangements.

NIH should maintain a policy of no out-of-pocket expenses to the patient.

Payment agreements should not affect participation in research.

AZT Safety Unchanged Following Review

As a result of unpublished data on the possible toxicity of perinatally administered AZT, NIAID brought together an independent panel on behalf of NIH to review data, summarize available information, and recommend research.

The panel included basic and clinical researchers, epidemiologists, HIV-infected women, and a bioethicist.

Two studies were at the center of the discussion. The first, an ongoing study by the National Cancer Institute (NCI), showed an increase in tumors in the offspring of mice given very high doses of AZT during days 12 to 18 of gestation.

Conducted by Glaxo-Wellcome, the second study showed no increase in carcinogenesis at doses simulating those of clinical practice.

The panel unanimously concluded that the known benefits of AZT in preventing perinatal HIV transmission appear to far outweigh the hypothetical concerns of transplacental carcinogenesis raised by the NCI study.

It emphasized the need for careful, long-term followup of all children exposed *in utero* to antiretroviral therapy, including those not HIV-infected.

For a full summary of the meeting, go to http://www.niaid.nih.gov/factsheets/aztsumm.htm.

AZT Panel-Recommended Research

Clinical

Enhance studies of the long-term effects of AZT in perinatally exposed children.

Improve awareness of the industry-sponsored Antiretroviral Pregnancy Registry in HIV-infected women and health care providers.

Study interventions that maximize safety and minimize likelihood of long-term side effects (several are under way).

Basic

Complete two-year followup of remaining mice in the NCI study.

Conduct further research of transplacental carcinogenesis of nucleoside analogs in mice, including mechanisms and dose dependency, and conduct confirmatory studies in at least one other species.

Study the significance of AZT incorporation into DNA and determine the relationship between AZT pharmacokinetics and incorporation.

NIAID and CDC—Distinct Roles in Emerging Diseases

Council heard two presentations defining the roles of NIAID and the Centers for Disease Control and Prevention to counter emerging diseases.

NIAID's perspective was given by Dr. Stephanie James, chief of the Parasitology and International Programs Branch, Division of Microbiology and Infectious Diseases (DMID).

Dr. Daniel Colley, director of the Division of Parasitic Diseases, National Center for Infectious Diseases, spoke for CDC.

Dr. James described NIAID's major research goals: improve prediction and prevention of future threats; develop therapeutics, vaccines, and other control strategies; and strengthen national capacity to detect and respond to new threats from infectious diseases.

NIH and CDC Roles in Emerging Infectious Diseases

NIH	*CDC*
Basic research	Surveillance
Pathogenesis	Identification of microbes
Research training	Initial response and containment
Diagnostics	Public information dissemination
Drug development	
Vaccines	

While presenting CDC's mission in emerging diseases, Dr. Colley showed the complementary roles of CDC and NIH (see box at left).

Whereas NIH grants go mostly to research institutions, CDC's monies fund largely state, local, and international public health organizations.

What Review Designations Mean

Confused about the assortment of terms NIH has used to indicate a study section's overall judgment of an application?

Forget "noncompetitive" and "disapproved"; these terms have been dropped.

Here is the current nomenclature and definitions.

Recommended - the study section recommends funding; the application gets a priority score and summary statement. Roughly the top half of applications being reviewed are recommended.

Unscored - the study section judges the application to be in the bottom half of applications being reviewed and therefore unlikely to be funded.

The application does not receive a priority score but is reviewed, and the applicant receives the reviewers' critiques. Occasionally, an unscored application is funded by a special action of an institute's advisory council.

Not Recommended for Further Consideration (NRFC) - the study section does not recommend funding; the application cannot be funded by an institute.

Effect of Review Designations

	Priority score	Summary statement	May be funded
Recommended	Yes	Full	Yes
Unscored	No	Partial	Yes
NRFC	No	Synopsis of problems	No

Giving a Talk on Biomedical Research? See NIH's New Communications Package

With the help of Council member Dr. Samuel Silverstein, NIH prepared a package of background information on NIH that represents the fruits of a Council resolution initiated by Dr. Silverstein last January.

The resolution that went to Dr. Varmus recommended that NIH Councils take a more active role in communicating the benefits of NIH-supported research. This past Council, Dr. Fauci cited Dr. Silverstein for raising the idea and following through with it.

Called "Talking About NIH," the packet was provided by NIH for distribution to the Councils of all institutes and centers.

We are posting Dr. Varmus' 1996 commencement address to Harvard University, taken from the package, in the tools section of the *Council News* Website (http://www.niaid.nih.gov/ncn/toolmain.htm).

To get the whole package, fill out the feedback form on the site (http://www.niaid. nih.gov/ncn/main.htm), stating that you want "Talking About NIH," and we'll mail it to you.

International Malaria Meeting

In January, a multinational malaria conference in Dakar, Senegal, drew participants from around the world.

About 120 malariologists participated in the meeting sponsored by NIH, the Pasteur Institute, the Wellcome Trust, the British Medical Research Council, and others.

Attending from NIH were director Dr. Harold Varmus, DMID director Dr. John La Montagne, and staff of DMID, NIAID's Laboratory of Parasitic Diseases, and the NIH Fogarty International Center.

The group split into eight focus groups to define the scientific knowledge needed to advance prevention and control and determine how to build collaborative research to obtain the necessary information.

Among the scientific initiatives that emerged are establishing collaborative research networks and enhancing Internet resources in Africa. In addition, Dr. Varmus proposed a multilateral initiative to solicit ideas for developing research networks, repositories, or collaborations.

A followup meeting will likely take place in Europe in mid-summer.

How Congress Affects NIH

Like other government agencies, NIH needs two kinds of legislation to operate: authorizing and appropriations.

The Senate and House both have authorizing and appropriations committees. Authorizing committees define what we are responsible for; appropriations committees set annual budgets.

Providing the legal authority for what we do, the NIH authorizing bill is considered every three years and is on the agenda of the 105th Congress. In contrast, NIH must have a new appropriations bill each year for work to continue.

The 105th Congress will take on many issues of importance to NIH. Likely topics are human fetal tissue research, genetics testing and privacy, human cloning, needle exchange, medical uses of marijuana, "mad cow" disease, hepatitis C and blood safety, and alternative medicine.

Another hot area is how NIH sets priorities, i.e., how it decides how much to fund different research areas and diseases.

Committee structure and composition have changed significantly in this Congress. For a chart showing NIH's authorizing and appropriations committees and their members, see this article in the News Section of our Website: http://www.niaid.nih.gov/ncn/news.htm.

RESEARCH *news*

Major NIAID Study Reduces Asthma in Children of the Inner City

The National Cooperative Inner-City Asthma Study is showing the benefits of a community-based intervention.

A key feature is the use of counselors to teach asthma self-management and help patients and their families institute environmental controls, such as removing allergens from their homes.

The approach was highly successful: asthma symptoms decreased significantly, with patients averaging two additional symptom-free weeks a year.

Conducted in eight centers, the study enrolled more than 1,000 high-risk children: 73 percent African-Americans, and 20 percent Latinos.

Following these promising results, a second study is already under way with new educational programs for patients and physicians and a stronger focus on environmental interventions.

The National Institute of Environmental Health Sciences and NIAID are cosponsoring the study, which will begin enrolling patients this summer or fall.

National Cooperative Drug Discovery Groups—HIV Awards

In response to program announcement 95-047, reissued in April 1996, NIAID awarded two new grants (of six applications) for therapeutics discovery research.

PA-95-047 was co-issued with the National Institute of Mental Health (NIMH) and the National Institute of Neurological Disorders and Stroke to solicit applications in 1995-1997.

In addition to the two grants funded by NIAID, a third grant was funded by NIMH, and part of a fourth, by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

Under the NCDDG-HIV program, interdisciplinary teams of investigators from academia and the private sector collaborate on the discovery and development of innovative therapeutic strategies against HIV infection and disease.

HIV Gene Therapy with RNA Inhibitors

Principal investigator: Dr. Eli Gilboa, Duke University Medical Center

This NCDDG-HIV focuses on developing gene therapy by transducing hematopoietic stem cells with potent RNA-based inhibitors of HIV. The group will develop novel reagents and methods to evaluate RNA-based HIV inhibitors in clinical studies.

Project 1 - **Dr. Bruce Sullenger**
Duke University Medical Center

Development of RNA-based inhibitors of HIV-1 expression and replication to be evaluated alone and in combination.

Project 2 - **Dr. Clayton Smith**
Duke University Medical Center

Transduction of umbilical cord stem cells; evaluation of RNA-based inhibitors in preclinical models of HIV-1 infection, including the SCID-hu mouse.

Project 3 - **Dr. Kenton Lohman**
Becton Dickinson, Inc.

Development of sensitive and specific *in situ* assays to quantitate gene-modified cells following transplantation to detect vector DNA and expressed RNA in transduced cells.

Capsid-Targeted Viral Inactivation

Principal investigator: Dr. Jef Boeke, Johns Hopkins University

This NCDDG-HIV focuses on a gene therapy strategy in which HIV proteins target an antiviral moiety to the virion. Genes for candidate antiviral proteins, including deleterious enzymes and mutant HIV proteins, will be fused to HIV genes, expressed intracellularly, and tested for the ability to disrupt virion integrity and, therefore, infectivity.

Project 1 - **Dr. Jef Boeke**
Johns Hopkins University

Use of capsid structural proteins (encoded by the *gag* gene) to deliver antiviral moieties to virions; design and preliminary evaluation of fusion constructs.

Project 2 - **Dr. Beatrice Hahn**
University of Alabama, Birmingham

Use of HIV and SIV accessory proteins Vpr, Vpx, and Vif to deliver antiviral moieties to virus particles; design and preliminary evaluation of fusion constructs.

Project 3 - **Dr. Gary Kurtzman**
Avigen, Inc.

Construction and production of high-titer, high-purity preparations of adeno-associated virus vectors containing antiviral fusion genes designed by Drs. Boeke and Hahn for evaluation in lymphocytes, macrophages, and ultimately hematopoietic stem cells.

Neuroprotection Through Inhibition of Oxidative Stress - funded by NIMH

Principal investigator: Dr. Leon Epstein, University of Rochester

The theme of this NCDDG-HIV is to identify compounds that block oxidative stress and NFκB activation, thus combining neuroprotection, anti-inflammatory, and (indirectly) antiretroviral strategies.

Project 1 - **Dr. Stephen Dewhurst**
University of Rochester

Investigation of the central role of NFκB in maintaining the chronic inflammatory process in the brain by upregulating HIV-1 and cellular (cytokine) gene expression in microglia and by promoting transendothelial migration of HIV-1 infected macrophages.

Project 2 - **Dr. Harris Gelbard**
University of Rochester

Pharmacological strategies to define the cellular pathways underlying oxidative stress in neuronal cultures, predicting that TNFα, platelet activating factor, arachidonic acid, and the toxic viral product HIV-1 Tat will decrease intracellular glutathione levels, increase reactive oxidative intermediates, and increase lipid peroxidation.

Project 3 - **Dr. Howard Gendelman**
University of Nebraska

Determination of the composition of neurotoxic products of HIV-1-infected microglia using high performance liquid chromatography coupled with radioimmunoassays and cytokine bioassays.

Project funded by NIDDK - **Dr. Alan Smith**
Aastrom Biosciences

Use of Aastrom Biosciences' technology to address the difficulty in maintaining and expanding hematopoietic stem and early progenitor cells *ex vivo* and in achieving reproducibly high transduction levels for gene transfer in these cells.

FEATURE *articles*

NIAID's Winter Policy Retreat Features View From the Outside

In December, the Institute held its annual Winter Policy Retreat, a key NIAID planning meeting. For the first time, an outside speaker broadened the perspective at the retreat, which brings together senior-level managers to discuss research priorities, review policy, and examine special issues.

Winter Policy Retreat Major Topics

Budget and funding policy

Future of NIAID's tuberculosis effort

Malaria research

Opportunities in tolerance

Managed Care Working Group

NIAID 50th anniversary

Jeffrey Bluestone on tolerance

Dr. Jeffrey Bluestone, director of the Ben May Institute and professor of the Department of Pathology of the University of Chicago, painted the big picture for opportunities in immunologic tolerance.

Dr. Bluestone is a leading researcher in tolerance, a field showing promise for translating basic research findings into clinical applications.

Calling his talk "T and B Cell Tolerance: The Last Frontier in Immunology Research," Dr. Bluestone showed why tolerance is ripe for scientific breakthroughs.

He told the group that, as knowledge grows about how tolerance works, we will move toward controlling immunologic problems such as allergies and graft rejection using immunomodulation instead of toxic, immunosuppressive drugs.

"Tolerance affects everything from transplantation to vaccination," Dr. Bluestone commented.

Focus group followed

NIAID's Division of Allergy, Immunology, and Transplantation (DAIT) took action following Dr. Bluestone's comments by holding a tolerance focus group in January at the 4th International Tolerance Induction Meeting in Breckenridge, Colorado.

Recommendations of the Tolerance Focus Group

Foster interinstitutional collaborations

Support research on surrogate markers for tolerance and rejection

Conduct regular focus group meetings

Facilitate collaborations between academia and industry; create incentives for companies

Promote reagent and animal exchange

The meeting highlighted actions the Institute could take to foster progress in tolerance research. For more on focus groups, see the article on the next page.

Following up on the meeting, DAIT plans to issue an FY 1998 program announcement, Basic and Clinical Research on Antigen-Specific Immune Tolerance, with a set-aside of $1.5 million.

Some of the other measures NIAID can undertake to develop the field are straightforward and involve little cost, such as enabling investigators to use the small grant (R03) for small projects.

Others requiring a bigger investment will take more careful consideration.

New studies planned

Collaborating with the Juvenile Diabetes Foundation International, NIAID will fund new clinical studies on diabetes. Inducing tolerance is especially important when diabetic patients receive either a pancreas or an islet cell transplant to ensure that the original autoimmune disease does not destroy the new tissue.

Currently, NIAID supports investigator-initiated research, program projects, and clinical trials to better understand tolerance and move new knowledge into clinical use.

In autoimmunity and transplantation, the Institute is supporting studies to pioneer innovative treatments for autoimmunity, induce donor-specific tolerance before a transplant, and further understanding of the basic mechanisms involved in peripheral tolerance.

Focus Groups Help Us Stay in Touch

During the past year, Dr. Fauci has been conducting what have come to be known as "focus group" meetings with outside scientists.

These popular forums let extramural scientists give candid feedback to NIAID.

The *ad hoc* gatherings have explored Institute interactions with investigators and industry, training, academic health centers, communications, congressional relations, and other topics.

"These meetings have been extremely useful to me and to the NIAID leadership," stated Dr. Fauci at Council.

He also plans to hold a focus group on minority issues, e.g., increasing the number of minority scientists successful in pursuing careers in biomedical research.

Divisions follow the lead

Following this success, staff in the Institute's Divisions have begun holding their own focus group meetings, reporting the outcomes at the Institute's Winter Policy Retreat.

As an example, DAIT director Dr. Robert A. Goldstein and some of his staff met last year with scientists from a range of organizations, including the American Academy of Allergy, Asthma, and Immunology; the American Association of Immunologists; and the Inter-American College of Physicians and Surgeons.

Investigators speak out

The meetings were so popular that all parties wanted a followup meeting this year.

Participants spoke their minds on many subjects, for example, training, funding, and review, offering concrete recommendations on how to better use small grants (R03) for investigators conducting small projects.

They also want Institute staff to be more proactive in advising applicants and grantees, especially those having difficulty getting funded.

NIAID came away with action items from the groups, for example, to include outside advisors earlier in the Institute's planning process.

A common thread running through all divisional focus group meetings was the community's relations with DRG, especially the level of expertise on study sections and the quality of reviews.

NIAID *Council News*

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